

3731. (New) The method of Claim 10, comprising treating a subject having overflow incontinence.

38. (New) The method of Claim 10, comprising treating a subject having passive incontinence.

39. (New) The method of Claim 10, comprising treating a subject having reflux incontinence.

40. (New) The method of Claim 10, comprising treating a subject having urge incontinence.

41. (New) The method of Claim 10, comprising treating a subject having urinary stress incontinence.--

*B4*  
*cont.*

#### REMARKS

Claims 10-35 are pending. Editorial revisions have been made to improve the clarity of the claim set. New Claims 21-35 find support in the specification at page 1, lines 30-35, page 32, lines 1-7 and on page 38, lines 2-7. Accordingly, the Applicants do not believe that any new matter has been added.

#### Rejection--Provisional Obviousness-type Double Patenting

Claims 1-20 were provisionally rejected over Claims 1-14 of copending (allowed) U.S. Application No. 09/646,878. This provisional rejection is moot for Claims 1-9, which have been canceled. Claims 10-35 are directed to compounds that are structurally distinct from the compounds recited by Claims 1-14 of the copending application. The compounds recited by present Claims 10-35 have general formulas IV, V, VI, VII or VIII. However, the compounds that are recited by Claims 1-14 of U.S. Application No. 09/646,878 correspond to general formula (I). Accordingly, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for early examination on the merits.

Respectfully submitted,

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MARKED-UP COPY OF AMENDMENT

IN THE CLAIMS

Cancel Claims 1-9.

Please amend Claims 10, 11, 13, 14, 15 and 17-20 as follows:

--10. (Amended) A method for the prophylactic and/or therapeutic treatment of dysuria that comprises:

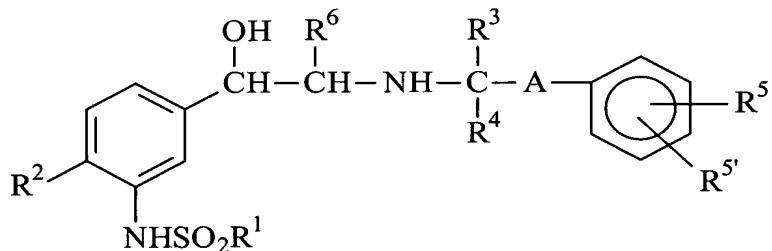
administering to a human being or an animal an effective amount of a compound, which is a  $\beta_3$  adrenergic receptor agonist, having a general formula selected from the group consisting of [selected from the group of consisting of a compound of] formula (IV), (V), (VI), (VII) and (VIII),

or a salt or prodrug thereof, or for the compound of formula (VII) an ester or amide thereof;

wherein

(a) [the] a compound of formula (IV) is represented by the following general formula:

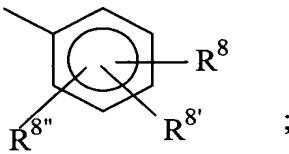
wherein



R<sup>1</sup> is lower alkyl, aryl or arylalkyl;

R<sup>2</sup> is hydrogen, hydroxy, alkoxy, -CH<sub>2</sub>OH, cyano, -C(O)OR<sup>7</sup>, -CO<sub>2</sub>H, -CONH<sub>2</sub>, tetrazole, -CH<sub>2</sub>NH<sub>2</sub> or halogen;

R<sup>3</sup> is hydrogen, alkyl, heterocycle or



$R^4$  is hydrogen, alkyl or B;

$R^5$ ,  $R^{5i}$ ,  $R^8$ ,  $R^{8i}$  and  $R^{8ii}$  are independently hydrogen, alkoxy, lower alkyl, halogen,  $-OH$ ,  $-CN$ ,  $-(CH_2)_nNR^6COR^7$ ,  $-CON(R^6)R^{6i}$ ,  $-CON(R^6)OR^{6ii}$ ,  $-CO_2R^6$ ,  $-SR^7$ ,  $-SOR^7$ ,  $-SO_2R^7$ ,  $-N(R^6)SO_2R^1$ ,  $-N(R^6)R^{6i}$ ,  $-NR^6COR^7$ ,  $-OCH_2CON(R^6)R^{6ii}$ ,  $-OCH_2CO_2R^7$  or aryl; or

$R^5$  and  $R^{5i}$  or  $R^8$  and  $R^{8i}$  may together with the carbon atoms to which they are attached form an aryl or heterocycle;

$R^6$  and  $R^{6i}$  are independently hydrogen or lower alkyl; and

$R^7$  is lower alkyl;

$R^9$  and  $R^{9i}$  are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

$R^9$  and  $R^{9i}$  may together with the nitrogen atom to which they are attached form a heterocycle;

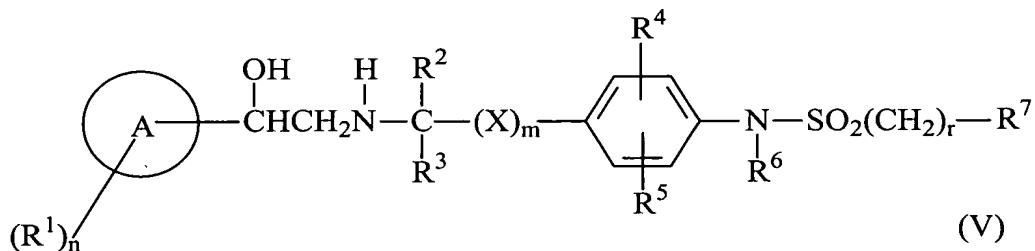
A is a bond,  $-(CH_2)_n-$  or  $-CH(B)-$ , wherein n is an integer of 1, 2 or 3 and

B is  $-CN$ ,  $-CON(R^9)R^{9i}-$  or  $-CO_2R^7$ ;

with the proviso that when A is a bond or  $-(CH_2)_n-$  and  $R^3$  is hydrogen or unsubstituted alkyl, then  $R^4$  is B or substituted alkyl;

(b) [the] a compound of formula (V) is represented by the following general formula:

wherein



n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

R<sup>1</sup> is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5) NR<sup>8</sup>R<sup>8</sup>, (6) SR<sup>8</sup>, (7) trifluoromethyl, (8) C<sub>1</sub>-C<sub>10</sub> alkyl, (9) OR<sup>8</sup>, (10) SO<sub>2</sub>R<sup>9</sup>, (11) OCOR<sup>9</sup>, (12) NR<sup>8</sup>COR<sup>9</sup>, (13) COR<sup>9</sup>, (14) NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, (15) NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>, or (16) C<sub>1</sub>-C<sub>10</sub> alkyl substituted by hydroxy, halogen, cyano, NR<sup>8</sup>R<sup>8</sup>, SR<sup>8</sup>, trifluoromethyl, OR<sup>8</sup>, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, NR<sup>8</sup>COR<sup>9</sup>, COR<sup>9</sup>, SO<sub>2</sub>R<sup>9</sup>, OCOR<sup>9</sup>, NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup> or NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>;

R<sup>2</sup> and R<sup>3</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl or (3) C<sub>1</sub>-C<sub>10</sub> alkyl with 1 to 4 substituents selected from hydroxy, C<sub>1</sub>-C<sub>10</sub> alkoxy, or halogen;

X is (1) -CH<sub>2</sub>-, (2) -CH<sub>2</sub>-, (3) -CH=CH- or (4) -CH<sub>2</sub>O-;

R<sup>4</sup> and R<sup>5</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) halogen, (4) NHR<sup>8</sup>, (5) OR<sup>8</sup>, (6) SO<sub>2</sub>R<sup>9</sup> or (7) NHSO<sub>2</sub>R<sup>9</sup>;

R<sup>6</sup> is (1) hydrogen or (2) C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sup>7</sup> is Z-(R<sup>1a</sup>)<sub>n</sub>;

R<sup>1a</sup> is (1) R<sup>1</sup>, (2) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup> or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo, R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup>, or halogen;

Z is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring;

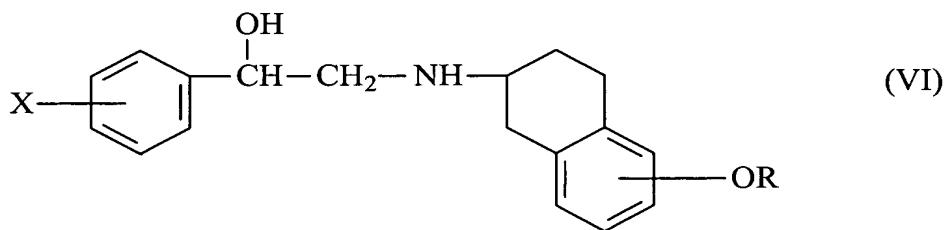
R<sup>8</sup> is (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo, NR<sup>10</sup>R<sup>10</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>1</sub>-C<sub>10</sub> alkylthio, and C<sub>1</sub>-C<sub>10</sub> alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO<sub>2</sub>H,

$\text{CO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{SO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_8$  cycloalkyl,  $\text{C}_1\text{-C}_{10}$  alkoxy, or  $\text{Z}$  optionally substituted by from 1 to 3 halogen,  $\text{C}_1\text{-C}_{10}$  alkyl or  $\text{C}_1\text{-C}_{10}$  alkoxy, or (5)  $\text{C}_1\text{-C}_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $\text{CO}_2\text{H}$ ,  $\text{CO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{SO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_8$  cycloalkyl,  $\text{C}_1\text{-C}_{10}$  alkoxy,  $\text{C}_1\text{-C}_{10}$  alkyl, or  $\text{Z}$  optionally substituted by from 1 to 4 halogen,  $\text{C}_1\text{-C}_{10}$  alkyl or  $\text{C}_1\text{-C}_{10}$  alkoxy;

$\text{R}^9$  is (1)  $\text{R}^8$  or (2)  $\text{NR}^8\text{R}^8$ ; and

$\text{R}^{10}$  is (1)  $\text{C}_1\text{-C}_{10}$  alkyl, or (2) two  $\text{R}^{10}$  groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with  $\text{C}_1\text{-C}_{10}$  alkyl;

(c) [the] a compound of formula (VI) is:

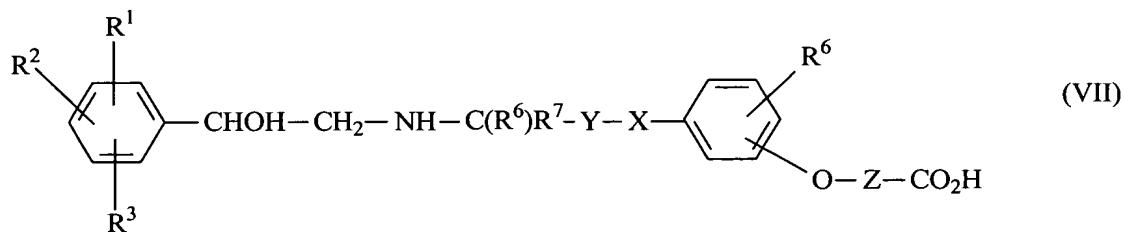


wherein

$\text{X}$  is hydrogen, halogen, trifluoromethyl or lower alkyl, and

$\text{R}$  is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of cyclo( $\text{C}_3\text{-C}_7$ )alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxy carbonyl; cyclo( $\text{C}_3\text{-C}_7$ )alkyl or lower alkanoyl;

(d) [the] a compound of formula (VII) is represented by the following general formula:



wherein

$R^1$  is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

$R^2$  is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

$R^3$  is a hydrogen, chlorine or bromine atom or a hydroxyl group,

$R^4$  is a hydrogen atom or a methyl group;

$R^5$  is a hydrogen atom or a methyl group;

$R^6$  is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

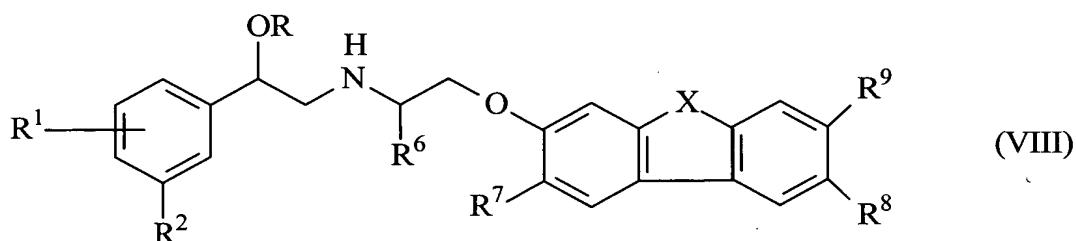
$X$  is an oxygen atom or a bond;

$Y$  is an alkylene group of up to 6 carbon atoms or a bond; and

$Z$  is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) [the] a compound of formula (VIII) is represented by the following general

formula:



wherein

$R$  is hydrogen or methyl,

$R^1$  is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,

$R^2$  is hydrogen, hydroxymethyl,  $-NHR^3$ ,  $-SO_2NR^4R^4'$  or nitro,

$R^3$  is hydrogen, methyl,  $-SO_2R^5$ , formyl or  $-CONHR^6$ ,

$R^4$  and  $R^4'$  are independently hydrogen, lower alkyl or benzyl,

$R^5$  is lower alkyl, benzyl or  $-NR^4R^4'$ ,

$R^6$  is hydrogen or lower alkyl,

$R^6'$  is hydrogen or lower alkyl,

$R^9$  is hydrogen, amino, acetylamino or hydroxy, and

$X$  is N, O, S or methylene;

provided that when X is N, O or S,  
then R<sup>9</sup> is hydrogen, either R<sup>7</sup> or R<sup>8</sup> is hydrogen, and the other is hydrogen, amino,  
acetylamino or hydroxy; and

provided that when X is methylene,  
then both R<sup>7</sup> and R<sup>8</sup> are hydrogen.

11. (Amended) The method of Claim 10 [that comprises] comprising administering  
[a  $\beta_3$  adrenergic receptor agonist] the compound of formula (IV) or a salt thereof.

13. (Amended) The method of Claim 10, comprising administering [a  $\beta_3$  adrenergic  
receptor shown by the following] the compound of formula (VI) or a salt thereof.

14. (Amended) The method of Claim 10, comprising administering [a  $\beta_3$  adrenergic  
receptor agonist shown by the following] the compound of formula (VII) or a salt, ester or  
amide thereof.

15. (Amended) The method of Claim 10, comprising administering [a  $\beta_3$  adrenergic  
receptor agonist shown by the following] the compound of formula (VIII) or a salt thereof.

17. A method for the prophylactic and/or the therapeutic treatment of pollakiuria or  
urinary incontinence comprising administering to a subject in need thereof an effective  
amount of the [ $\beta_3$  adrenergic receptor agonist] compound as defined in [of] Claim 10 or a  
pharmaceutically acceptable salt thereof.

18. (Amended) A method for the prophylactic and/or the therapeutic treatment of  
nervous pollakiuria, neurogenic bladder dysfunction, nocturia, unstable bladder, cystospasm,  
chronic cystitis, chronic prostatitis, overflow incontinence, passive incontinence, reflex  
incontinence, urge incontinence, urinary stress incontinence comprising administering to a  
subject in need thereof an effective amount of [the  $\beta_3$  adrenergic receptor agonist] a  
compound as defined in [of] Claim 10 or a pharmaceutically acceptable salt thereof.

19. (Amended) A commercial package comprising:

the compound [of] as defined in Claim 10

written matter associated therewith,

wherein the written matter states that the pharmaceutical composition can or should  
be used for preventing and/or treating dysuria.

20. (Amended) An article of manufacture comprising:

a packaging material and

the compound [of] as defined in Claim 10,  
wherein said packaging material comprises a label or a written material which  
indicates that the compound [identified] defined in Claim 10 can or should be used for  
preventing and/or treating dysuria.--

Add new Claims 21-35:

--21.-35. (New)--